UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/749,528	12/30/2003	Xing Su	INTEL1210/US (P18026)	8863

28213 7590 03/24/2006

DLA PIPER RUDNICK GRAY CARY US, LLP
4365 EXECUTIVE DRIVE
SUITE 1100
SAN DIEGO, CA 92121-2133

EXAMINER	
YU, MELANIE J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 03/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/749,528	SU ET AL.	
	Examiner	Art Unit	
	Melanie Yu	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-25,27-33 and 38-58* is/are pending in the application.

4a) Of the above claim(s) *39-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-25,27-33 and 38* is/are rejected.

7)☒ Claim(s) *2-25,27-33 and 38* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/17*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 19 January 2006 has been entered.

Election/Restrictions

2. Newly submitted claims 39-58 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the invention of group a) claims 2-25, 27-33 and 38 and group b) claims 39-58 are drawn to different embodiments of a method for analyzing protein content.

3. Inventions of group a and group b are directed to related methods for analyzing protein content. The related inventions are distinct if the inventions as claimed do not overlap in scope, i.e., are mutually exclusive; the inventions as claimed are not obvious variants; and the inventions as claimed are either not capable of use together or can have a materially different design, mode of operation, function, or effect. See MPEP § 806.05(j). In the instant case, the methods are mutually exclusive, are not obvious variants and have a materially different modes of operation because the method of group a requires depositing each fraction at a discrete location on a solid substrate, which is not required of the method of group b, and the method of group b requires depositing each fraction at a discrete location within at least one stream of flowing liquid in a microfluidic device, which is not required of method of group a. Therefore,

because the groups require different deposition locations, the methods are mutually exclusive, not obvious variants and have materially different modes of operation.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 39-58 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Objections

4. Claims 2-25, 27-33 and 38 are objected to because of the following informalities: claims 2-25, 27-33 may not depend from a claim that occurs after the dependent claims and must depend from a claim that is chronologically before the dependent claims. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 2-25, 27-33 and 38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Amended claim 38 recites the phrase "each fraction containing an individual protein or protein fragment". The original specification fails to provide sufficient support for a plurality of fractions, wherein each fraction contains an individual protein. It is noted that at

paragraph 36, the specification teaches proteins or protein fragments in a sample separated according to their chemical and physical properties and are then maintained in a separated state, but does not specify that each fraction resulting from the separation contains an individual protein or protein fragment.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 2-25, 27-33 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 38 recites the phrase "each fraction containing an individual protein or protein fragment", which is vague because it is unclear whether the fraction contains a single protein or protein fragment, a plurality of the same protein or protein fragment, whether a single type of protein or protein fragment (ie. proteins that are the same size), are present in the fraction, or whether a protein or protein fragment must be present in the fraction, and the total number of proteins/protein fragments is irrelevant.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

7. Claim 2-5, 10, 14-17, 20-26, 29-33 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natan et al. (US 6,242,264) in view of Natan et al. (US 6,579,721).

Natan et al. ('264) teach a method comprising: chromatographically separating proteins and protein fragments (biomolecule is protein and therefore the eluate contains proteins, col. 36, lines 32-56), wherein each fraction containing an individual protein (individual proteins are

present in the fraction and therefore each fraction contains an individual protein; col. 36, lines 32-56) in a sample into a plurality of fractions (col. 35, lines 28-40) and depositing each fraction at a discrete location on a solid substrate to create a plurality of discrete protein enriched locations (col. 35, lines 30-35) for Raman spectra detection (SERS is Raman scattering and produces a Raman spectra, col. 35, lines 30-34), but fail to teach the specific method steps of Raman detection requiring contacting proteins with a capture probe and contacting a probe/protein complex with a Raman-active probe.

Natan et al. ('721) teach a method for analyzing the protein content of a biological sample (col. 10, lines 40-47 describe the sandwich assay; col. 10, line 52 describes the target analyte being a protein), comprising: depositing proteins in a separated state at discrete locations on a solid substrate (ligands are attached at specific locations, therefore ligands can be samples in each well which are maintained without cross contamination, col. 25, lines 1-4); contacting the separated proteins deposited at the plurality of discrete protein enriched locations with probes under conditions suitable to form a capture probe/protein complex at one or more of the discrete locations (col. 3, lines 47-54; col. 10, lines 58-64; at col. 13, lines 45-52 any one of the participants can be immobilized to the substrate surface, a ligand is then bound to the immobilized receptor, protein); contacting the complexes with a Raman-active probe construct that binds to the complex (col. 3, lines 54-63; col. 13, lines 45-52, an Au-conjugated antibody is conjugated with the ligand, which is bound to the immobilized receptor, protein); and detecting Raman spectra produced by the probe construct/protein complexes at the plurality of discrete locations, wherein a Raman spectrum from at a discrete location provides information about the chemical composition of a protein the corresponding discrete protein enriched location by

analyzing the protein content of a complex biological sample (col. 23, lines 58-61 discloses SERS detection; Fig. 12 discloses an amplified detection after an unamplified detection; furthermore a change in resonance is detected as the target is brought in contact with the Raman-active probe, therefore the SERS detection occurs before and after contacting the proteins with capture probes and Raman active probes, col. 18, lines 1-5; surface chemical interactions are analyzed, col. 35, lines 1-5; compounds are identified, col. 24, lines 1-5), in order to provide simultaneous detection of multiple target analytes using a solid support.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the detection of Natan et al. ('264), the Raman detection method steps as taught by Natan et al. ('721), in order to provide increased sensitivity and accuracy of SERS detection.

With respect to claims 3-5, Natan et al. ('721) teaches the capture probe being a primary antibody that binds specifically to the protein in the complex (immobilized receptor is a protein, primary antibody is ligand, col. 13, lines 45-52), and the Raman-active probe construct comprising a secondary antibody as probe and a Raman tag (secondary antibody is antibody conjugated to Au, col. 13, lines 50-52). Natan et al. ('721) also teaches the Raman-active probe being a composite organic-inorganic nanoparticle (organic portion is the secondary antibody conjugated to the inorganic portion of gold or silver particle; col. 15, lines 28-29).

With respect to claim 10, 14-17, Natan et al. ('721) teach a substrate coated with one or more organic or inorganic materials prior to immobilization of proteins (gold evaporated onto glass substrate, col. 24, lines 40-44). Natan et al. ('721) further teaches the substrate comprised of a plurality of discrete locations on a flat plate (wells, col. 24, line 66-col. 25, line 5), and

detection automated to accomplish high throughput scanning at a plurality of discrete protein enriched locations (col. 23, lines 63-66; col. 26, lines 39-48). Natan et al. ('721) also teaches the substrate comprising gold (gold evaporated on glass; col. 24, lines 41-44) and contacting the proteins at the discrete locations with silver nanoparticles (col. 16, lines 45-53).

Regarding claims 20-26, Natan et al. ('721) teach the Raman spectra being a SERS spectra (col. 23, lines 58-61), and collecting the SERS spectra from the discrete locations to compile a protein profile of the sample (col. 25, lines 1-5) and the Raman spectra and locations of the proteins on the solid substrate are recorded and correlated (col. 23, line 62-col. 24, line 7). Natan et al. ('721) further teach collection being automated to accomplish high throughput SERS spectra screening of the discrete locations (SERS can be used as well as SPR using the PDMS microwell arrays for high throughput screening, col. 23, lines 58-61). Natan et al. ('721) also teach the spectrum containing information regarding a protein characteristic of identification of the protein (sensors are used to detect unique compounds, which can be proteins, col. 24, lines 1-5). Maintaining the separated proteins in a separated state comprises depositing each fraction at a discrete location within at least one stream of flowing liquid in a microfluidic system to create a plurality of discrete protein enriched locations (proteins are separated and introduced to a flow cell in order to immobilize to a substrate, col. 29, lines 29-52). Further comprising mixing the stream of flowing liquids comprising the separated proteins with a stream of flowing metal colloids by combining streams under conditions suitable for contacting the separated proteins with the metal colloids and the detection is SERS detection (nanoparticles introduced into flow cell where the stream of separated proteins are already located, col. 29, lines 4-52).

With respect to claims 2 and 29-33, Natan et al. ('721) teach a sample being a patent sample of blood (col. 15, lines 15-23). Natan et al. ('721) also teach creating a protein profile of the sample based on data obtained from the Raman spectra (col. 23, lines 58-61; col. 24, lines 1-6), and repeating the method using a variety of different patient samples to create a protein library containing a plurality of different protein profiles (sensor combine to form a library of ingredients, proteins, in the sample, col. 24, lines 4-6). Natan et al. ('721) further teach the comparing the protein profile of the sample with one or more protein profiles of the library to detect a difference indicative of a disease (asthma, col. 15, lines 23-31).

8. Claim 2-5, 10, 14-17, 20-26, 29-33 and 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hess et al. (US 6,716,629) in view of Natan et al. (US 6,579,721).

Hess et al. teach a method comprising: chromatographically separating proteins and protein fragments in a sample into a plurality of fractions, wherein each fraction contains an individual protein (sample is prepared using HPLC and liquid eluted from the chromatographic is deposited on a substrate and therefore a plurality of fractions are present, col. 57, lines 5-17; antigen is the analyte and binds to an antibody probe col. 45, lines 53-55, and analyte is in the sample and in the eluate fractions, col. 41, lines 41, lines 8-10) and depositing each fraction at a discrete location on a solid substrate to create a plurality of proteins in a separated state (equi-volume samples are stored on an array and therefore the plurality of proteins are stored in a separated state, col. 57, lines 7-17), wherein detection of the proteins in the eluate is performed by detection of a Raman spectra (col. 41, line 66-col. 42, line 11). Hess et al. fail to teach the specific detection method of detection by Raman spectra.

Natan et al. teach a method for analyzing the protein content of a biological sample (col. 10, lines 40-47 describe the sandwich assay; col. 10, line 52 describes the target analyte being a protein), comprising: separating proteins in a sample (separates target analyte based on chemical interaction, col. 23, lines 45-48; ligands for different target analyte must be separated in order for attachment at specific locations, col. 3, lines 23-26; ligands can be proteins, col. 10, lines 40-47); depositing proteins in a separated state at discrete locations on a solid substrate (ligands are attached at specific locations, therefore ligands can be samples in each well which are maintained without cross contamination, col. 25, lines 1-4); contacting the separated proteins deposited at the plurality of discrete protein enriched locations with probes under conditions suitable to form a capture probe/protein complex at one or more of the discrete locations (col. 3, lines 47-54; col. 10, lines 58-64; at col. 13, lines 45-52 any one of the participants can be immobilized to the substrate surface, a ligand is then bound to the immobilized receptor, protein); contacting the complexes with a Raman-active probe construct that binds to the complex (col. 3, lines 54-63; col. 13, lines 45-52, an Au-conjugated antibody is conjugated with the ligand, which is bound to the immobilized receptor, protein); and detecting Raman spectra produced by the probe construct/protein complexes at the plurality of discrete locations, wherein a Raman spectrum from at a discrete location provides information about the chemical composition of a protein the corresponding discrete protein enriched location by analyzing the protein content of a complex biological sample (col. 23, lines 58-61 discloses SERS detection; Fig. 12 discloses an amplified detection after an unamplified detection; furthermore a change in resonance is detected as the target is brought in contact with the Raman-active probe, therefore the SERS detection occurs before and after contacting the proteins with capture probes and

Raman active probes, col. 18, lines 1-5; surface chemical interactions are analyzed, col. 35, lines 1-5; compounds are identified, col. 24, lines 1-5), in order to provide simultaneous detection of multiple target analytes using a solid support.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the detection of proteins in an eluate of Hess et al., chromatographic separating compounds into a plurality of fractions, the Raman detection method steps as taught by Hess et al., in order to provide increased sensitivity and accuracy of SERS detection.

With respect to claims 3-5, Natan et al. teaches the capture probe being a primary antibody that binds specifically to the protein in the complex (immobilized receptor is a protein, primary antibody is ligand, col. 13, lines 45-52), and the Raman-active probe construct comprising a secondary antibody as probe and a Raman tag (secondary antibody is antibody conjugated to Au, col. 13, lines 50-52). Natan et al. also teaches the Raman-active probe being a composite organic-inorganic nanoparticle (organic portion is the secondary antibody conjugated to the inorganic portion of gold or silver particle; col. 15, lines 28-29).

With respect to claim 10, 14-17, Natan et al. teach a substrate coated with one or more organic or inorganic materials prior to immobilization of proteins (gold evaporated onto glass substrate, col. 24, lines 40-44). Natan et al. further teaches the substrate comprised of a plurality of discrete locations on a flat plate (wells, col. 24, line 66-col. 25, line 5), and detection automated to accomplish high throughput scanning at a plurality of discrete protein enriched locations (col. 23, lines 63-66; col. 26, lines 39-48). Natan et al. also teaches the substrate

comprising gold (gold evaporated on glass; col. 24, lines 41-44) and contacting the proteins at the discrete locations with silver nanoparticles (col. 16, lines 45-53).

Regarding claims 20-26, Natan et al. teach the Raman spectra being a SERS spectra (col. 23, lines 58-61), and collecting the SERS spectra from the discrete locations to compile a protein profile of the sample (col. 25, lines 1-5) and the Raman spectra and locations of the proteins on the solid substrate are recorded and correlated (col. 23, line 62-col. 24, line 7). Natan et al. further teach collection being automated to accomplish high throughput SERS spectra screening of the discrete locations (SERS can be used as well as SPR using the PDMS microwell arrays for high throughput screening, col. 23, lines 58-61). Natan et al. also teach the spectrum containing information regarding a protein characteristic of identification of the protein (sensors are used to detect unique compounds, which can be proteins, col. 24, lines 1-5). Maintaining the separated proteins in a separated state comprises depositing each fraction at a discrete location within at least one stream of flowing liquid in a microfluidic system to create a plurality of discrete protein enriched locations (proteins are separated and introduced to a flow cell in order to immobilize to a substrate, col. 29, lines 29-52). Further comprising mixing the stream of flowing liquids comprising the separated proteins with a stream of flowing metal colloids by combining streams under conditions suitable for contacting the separated proteins with the metal colloids and the detection is SERS detection (nanoparticles introduced into flow cell where the stream of separated proteins are already located, col. 29, lines 4-52).

With respect to claims 2 and 29-33, Natan et al. teach a sample being a patent sample of blood (col. 15, lines 15-23). Natan et al. also teach creating a protein profile of the sample based on data obtained from the Raman spectra (col. 23, lines 58-61; col. 24, lines 1-6), and repeating

the method using a variety of different patient samples to create a protein library containing a plurality of different protein profiles (sensor combine to form a library of ingredients, proteins, in the sample, col. 24, lines 4-6). Natan et al. further teach the comparing the protein profile of the sample with one or more protein profiles of the library to detect a difference indicative of a disease (asthma, col. 15, lines 23-31).

9. Claims 6-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natan et al. (US 6,242,264) in view of Natan et al. (US 6,579,721), as applied to claim 38, further in view of Grow (US 6,040,191).

Natan et al. ('264) in view of Natan et al. ('721), as applied to claim 38, teach a method for analyzing protein content of a biological sample, but fail to teach denaturing proteins in the sample.

Grow teaches contacting proteins in a sample prior with a denaturing agent denaturing proteins in a sample (chemicals are denaturing agent, col. 18, lines 54-58; col. 11, lines 14-20 and 26-42), in order to determine different unique structures of biological conformation of a biological-analyte complex.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of Natan et al. ('264) in view of Natan et al. ('721), denaturing proteins before separation as taught by Grow, in order to prevent false responses due to proteins being denatured, inactivated, poisoned or leached.

Regarding claim 6, Grow teaches a biological-analyte, protein, solubilized in an aqueous solution (col. 20, lines 32-39).

With respect to claims 8 and 9, Grow teaches a denaturing agent being surfactants (col. 56, lines 28-31), and denatured proteins dried on a substrate prior to detection of signals (col. 25, line 56-col. 26, line 5).

10. Claims 11-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natan et al. (US 6,242,264) in view of Carron (US 6,579,721), as applied to claim 38, further in view of Avseenko et al. (Immobilization of Proteins in Immunochemical Microarrays Fabricated by Electrospray Deposition, Analytical Chemistry, 2001, 73, 6047-6052).

Natan et al. ('264) in view of Natan et al. ('721), as applied to claim 38, teach a method for analyzing protein content of a biological sample without denaturing, but fail to teach separated proteins deposited using wet electrospray.

Avseenko et al. teach separated proteins deposited without denaturing using wet electrospray deposition (pg. 6048, right column, *Fabrication of Microarrays*, electrospray deposition of protein) onto an aluminum substrate (pg. 6048, left column, *Materials*, aluminized mylar film), in order to fabricate protein microarrays for immunochemical analysis.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of Natan et al. ('264) in view of Natan et al. ('721), deposition of proteins without denaturing using wet electrospray deposition as taught by Avseenko et al., in order to reduce spot size, increase fabrication rate, and simultaneously manufacture thousands of identical microchips while retaining ability to specifically bind antibodies.

Avseenko et al. also teach less preferable alternatives to deposition of proteins including contact writing (microcontact printing, pg. 6047, last paragraph left column-first paragraph, right column).

11. Claims 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natan et al. (US 6,242,264) in view of Natan et al. (US 6,579,721), as applied to claim 38, further in view of Storhoff et al. (US 2004/0053222).

Natan et al. ('264) in view of Natan et al. ('721), as applied to claim 38, teach a method for analyzing protein content of a biological sample, but fail to teach contacting nanoparticles with at least one chemical enhancer salt.

Storhoff et al. teach gold nanoparticles contacted with at least one chemical enhancer salt of LiCl (paragraph 0049), in order to allow a sufficient number of additional polyanionic polymer conjugates, wherein the polymer conjugates are proteins (paragraph 0053), to bind to the nanoparticles.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of Natan et al. ('264) in view of Natan et al. ('721), nanoparticles contacted with a solution containing at least one chemical enhancer salt as taught by Storhoff et al., in order to increase stability of nanoparticles while binding proteins.

12. Claims 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natan et al. (US 6,242,264) in view of Natan et al. (US 6,579,721), as applied to claim 38, further in view of Nelson et al. (US 5,955,729).

Natan et al. ('264) in view of Natan et al. ('721), as applied to claim 38, teach a method for analyzing protein content of a biological sample, but fail to teach analyzing separated proteins by mass spectroscopy.

Nelson et al. teach performing surface plasmon resonance-mass spectroscopy by detecting particles using SPR to detect the changes in the refractive index of the solution close to the surface of the sensor chip, and analyzing separated proteins by mass spectroscopy, to identify the presence of non-targeted ligands and to correct them for quantitative techniques.

Therefore it would have been obvious to one having ordinary skill in the art at the time the invention was made to include in the method of Natan et al. ('264) in view of Natan et al. ('721), analyzing separated proteins by mass spectroscopy as taught by Nelson et al., in order to quantify the amount of analyte in the sample and to provide real-time information regarding molecular interactions.

Nelson et al. teach compiling data from the mass spectroscopy with data from SPR (Fig. 4, relative intensity and resonance signals are compared, col. 4, lines 58-64), and according to Natan et al. an SERS measurement can be used instead of an SPR measurement in order to accommodate other surface-sensitive analytical techniques (col. 23, lines 54-61).

Response to Arguments

13. Applicant's arguments with respect to claims 2-25, 26-33 and 38 under 35 USC 103(a) have been considered but are moot in view of the new ground(s) of rejection. Previous rejections under 35 USC 103(a) have been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of the limitation requiring chromatographically separating

proteins and protein fragments in a sample into fractions prior to depositing the fractions on the solid substrate.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melanie Yu whose telephone number is (571) 272-2933. The examiner can normally be reached on M-F 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Melanie Yu
Patent Examiner
Art Unit 1641

BAO-THUY L. NGUYEN
PRIMARY EXAMINER
3/18/06.